Brief Contents

PART ONE	■ QUESTIONS Introducing Developmental Biology 1
CHAPTER 1	Comprehending Development: Generating New Cells and Organs 5
CHAPTER 2	Differential Gene Expression in Development 31
CHAPTER 3	Cell-Cell Communication in Development 69
PART TWO	■ SPECIFICATION Introducing Cell Commitment and Early Embryonic Development 107
CHAPTER 4	Fertilization: Beginning a New Organism 117
CHAPTER 5	Early Development: Rapid Specification in Snails and Nematodes 153
CHAPTER 6	The Genetics of Axis Specification in Drosophila 179
CHAPTER 7	Sea Urchins and Tunicates: Deuterostome Invertebrates 217
CHAPTER 8	Early Development in Vertebrates: Amphibians and Fish 241
CHAPTER 9	Early Development in Vertebrates: Birds and Mammals 285
RT THREE	■ THE STEM CELL CONCEPT Introducing Organogenesis 319
CHAPTER 10	The Emergence of the Ectoderm: Central Nervous System and Epidermis 333
CHAPTER 11	Neural Crest Cells and Axonal Specificity 375
CHAPTER 12	Paraxial and Intermediate Mesoderm 415
CHAPTER 13	Lateral Plate Mesoderm and the Endoderm 449
CHAPTER 14	Development of the Tetrapod Limb 489
CHAPTER 15	Sex Determination 519
CHAPTER 16	Postembryonic Development: Metamorphosis, Regeneration, and Aging 549
CHAPTER 17	The Saga of the Germ Line 591
PART FOUR	■ SYSTEMS BIOLOGY Expanding Developmental Biology to Medicine, Ecology, and Evolution 627
CHAPTER 18	Birth Defects, Endocrine Disruptors, and Cancer 635
CHAPTER 19	Ecological Developmental Biology: Biotic, Abiotic, and Symbiotic Regulation of Development 663
CHAPTER 20	Developmental Mechanisms of Evolutionary Change 689

Contents

PART ONE QUESTIONS

Introducing Developmental Biology 1

CHAPTER 1

Comprehending Development

Generating New Cells and Organs 5

The Cycle of Life 6

A Frog's Life 6

Gametogenesis and fertilization 6

Cleavage and gastrulation 7

Organogenesis 10

Metamorphosis and gametogenesis 11

"How Are You?" 12

Comparative embryology 12

Epigenesis and preformation 12

Naming the parts: The primary germ layers and early organs 14

The four principles of Karl Ernst von Baer 15

Keeping Track of Moving Cells: Fate Maps and Cell Lineages 17

Fate maps 19

Direct observation of living embryos 19

Dye marking 19

Genetic labeling 19

Transgenic DNA chimeras 23

Evolutionary Embryology 23

Embryonic homologies 25

Medical Embryology and Teratology 27

Genetic malformations and syndromes 27

Disruptions and teratogens 27

CHAPTER 2

Differential Gene Expression in Development 31

Evidence for Genomic Equivalence 32

■ SIDELIGHTS & SPECULATIONS The Basic Tools of Developmental Genetics 32

Differential Gene Transcription 34

Anatomy of the gene: Active and repressed chromatin 35

Anatomy of the gene: Exons and introns 35

Anatomy of the gene: Promoters and enhancers 37

Enhancer functioning 39

Transcription factor function 43

Keeping the right genes on or off 45

■ SIDELIGHTS & SPECULATIONS Reprogramming Cells: Changing Cell Differentiation through Embryonic Transcription Factors 46

Mechanisms of Differential Gene Transcription 47

Finding DNA regulatory sequences 48

Differentiated proteins from high and low CpGcontent promoters 48

DNA methylation, another key on/off switch of transcription 49

"Poised" chromatin 51

■ SIDELIGHTS & SPECULATIONS Genomic Imprinting and DNA Methylation 52

Differential RNA Processing 53

SIDELIGHTS & SPECULATIONS X Chromosome Inactivation: Noncoding RNAs in Transcriptional Gene Regulation 54

Creating families of proteins through differential nRNA splicing 56

Splicing enhancers and recognition factors 57

Control of Gene Expression at the Level of Translation 59

Differential mRNA longevity 59

Stored oocyte mRNAs: Selective inhibition of mRNA translation 59

Ribosomal selectivity: Selective activation of mRNA translation 61

microRNAs: Specific regulation of mRNA translation and transcription 61

Control of RNA expression by cytoplasmic localization 64

Posttranslational Regulation of Gene Expression 65

Coda 65

CHAPTER 3

Cell-Cell Communication in Development 69

Cell Adhesion 70

Differential cell affinity 70

The thermodynamic model of cell interactions 71 Cadherins and cell adhesion 72

■ SIDELIGHTS & SPECULATIONS Shape Change and Epithelial Morphogenesis: "The Force Is Strong in You" 76

Cell Migration 78

Cell Signaling 79

Induction and competence 79 Reciprocal induction 81

Epithelial-mesenchymal interactions 82

Paracrine Factors: Inducer Molecules 84

Signal transduction cascades: The response to inducers 84

Fibroblast growth factors and the RTK pathway 84

The JAK-STAT pathway 86

The Hedgehog family 88

The Wnt family 90

The TGF-β superfamily 92

■ SIDELIGHTS & SPECULATIONS Cell Death Pathways 94

Other paracrine factors 96

Juxtacrine Signaling 96

The Notch pathway: Juxtaposed ligands and receptors 96

■ SIDELIGHTS & SPECULATIONS Juxtacrine Signaling and Cell Patterning 97

The Extracellular Matrix as a Source of **Developmental Signals 99**

Integrins: Receptors for extracellular matrix molecules 100

The Epithelial-Mesenchymal Transition 101 The Cell Biology of Paracrine Signaling 102 Coda 104

PART TWO SPECIFICATION

Introducing Cell Commitment and Early Embryonic Development 107

Levels of Commitment 107 **Autonomous Specification 109** Conditional Specification 110

Morphogen Gradients and Conditional Specification 113

Syncytial Specification 114

CHAPTER 4

Fertilization

Beginning a New Organism 117

Structure of the Gametes 117

Sperm 117

Sperm anatomy 118

The egg 120

Recognition of egg and sperm 123

External Fertilization in Sea Urchins 124

Sperm attraction: Action at a distance 124

The acrosome reaction 125

Recognition of the egg's extracellular coat 126

Fusion of the egg and sperm cell membranes 128

One egg, one sperm 128

Summary 115

The fast block to polyspermy 129

The slow block to polyspermy 130

Calcium as the initiator of the cortical granule reaction 132

Activation of Egg Metabolism in Sea Urchins 134

Release of intracellular calcium ions 134

■ SIDELIGHTS & SPECULATIONS Rules of Evidence: "Find It, Lose It, Move It" 136

Effects of calcium release 137

Fusion of Genetic Material in Sea Urchins 139 Internal Fertilization in Mammals 140

Getting the gametes into the oviduct: Translocation and capacitation 141

In the vicinity of the oocyte: Hyperactivation, thermotaxis, and chemotaxis 143

The acrosome reaction and recognition at the zona pellucida 143

Gamete fusion and the prevention of polyspermy 145 Fusion of genetic material 146

Activation of the mammalian egg 146

■ SIDELIGHTS & SPECULATIONS The Nonequivalence of Mammalian Pronuclei 148

Coda 149

CHAPTER 5

Early Development Rapid Specification in Snails and Nematodes 153

Developmental Patterns among the Metazoa 153

Sponges and the diploblastic animals 154 The triploblastic animals: Protostomes and

The triploblastic animals: Protostomes and deuterostomes 155

EARLY DEVELOPMENTAL PROCESSES: AN OVERVIEW 155

Cleavage 155

From fertilization to cleavage 156 The cytoskeletal mechanisms of mitosis 157 Patterns of embryonic cleavage 158

Gastrulation and Axis Formation 158

EARLY DEVELOPMENT IN SNAILS 161

Cleavage in Snail Embryos 161

The snail fate map 164

Autonomous cell specification and the polar lobe 164

■ SIDELIGHTS & SPECULATIONS Adaptation by Modifying Embryonic Cleavage 167

Gastrulation in Snails 169

THE NEMATODE C. ELEGANS 170

Cleavage and Axis Formation in C. elegans 171

Rotational cleavage of the egg 171 Anterior-posterior axis formation 171 Dorsal-ventral and right-left axis formation 172 Control of blastomere identity 173

Gastrulation in C. elegans 176

CHAPTER 6

The Genetics of Axis Specification in Drosophila 179

EARLY DROSOPHILA DEVELOPMENT 179

Fertilization 180

Cleavage 180

The mid-blastula transition 182

GENES THAT PATTERN THE DROSOPHILA BODY PLAN 185

Primary Axis Formation during Oogenesis 186

Anterior-posterior polarity in the oocyte 186 Dorsal-ventral patterning in the oocyte 186

Generating the Dorsal-Ventral Pattern in the Embryo 190

Dorsal, the ventral morphogen 190 Establishing a nuclear Dorsal gradient 190 Effects of the Dorsal protein gradient 191

■ SIDELIGHTS & SPECULATIONS The Left-Right and Inside-Out Axes 193

Segmentation and the Anterior-Posterior Body Plan 194

Maternal gradients: Polarity regulation by oocyte cytoplasm 194

The molecular model: Protein gradients in the early embryo 194

The anterior organizing center: The Bicoid and Hunchback gradients 199

The terminal gene group 201

Summarizing early anterior-posterior axis specification in *Drosophila* 201

Segmentation Genes 202

Segments and parasegments 202 The gap genes 203

The pair-rule genes 204

The segment polarity genes 206

The Homeotic Selector Genes 209

Initiating and maintaining the patterns of homeotic gene expression 211

Realisator genes 211

Axes and Organ Primordia: The Cartesian Coordinate Model 212

Coda 213

CHAPTER 7

Sea Urchins and Tunicates

Deuterostome Invertebrates 217

EARLY DEVELOPMENT IN SEA URCHINS 217

Sea Urchin Cleavage 217

Blastula formation 219

Fate maps and the determination of sea urchin blastomeres 219

Gene regulatory networks and skeletogenic mesenchyme specification 221

Specification of the vegetal cells 224

Axis specification 225

Sea Urchin Gastrulation 225

Ingression of the skeletogenic mesenchyme 226 Invagination of the archenteron 229

EARLY DEVELOPMENT IN TUNICATES 232

Tunicate Cleavage 232

The tunicate fate map 233

Autonomous and conditional specification of tunicate blastomeres 234

Specification of the embryonic axes 236

Gastrulation in Tunicates 237

Coda 238

CHAPTER 8

Early Development in Vertebrates

Amphibians and Fish 241

EARLY AMPHIBIAN DEVELOPMENT 241

Fertilization, Cortical Rotation, and Cleavage 242

Unequal radial holoblastic cleavage 242

The mid-blastula transition: Preparing for gastrulation 245

Amphibian Gastrulation 245

Vegetal rotation and the invagination of the bottle cells 245

Epiboly of the prospective ectoderm 250

Progressive Determination of the Amphibian Axes 251

Specification of the germ layers 251

The dorsal-ventral and anterior-posterior axes 251

The Work of Hans Spemann and Hilde Mangold 252

Autonomous specification versus inductive interactions 252

Primary embryonic induction 254

Molecular Mechanisms of Amphibian Axis Formation 256

How does the organizer form? 256

Functions of the organizer 261

Induction of neural ectoderm and dorsal mesoderm: BMP inhibitors 262

Epidermal inducers: The BMPs 264

SIDELIGHTS & SPECULATIONS BMP4 and Geoffroy's Lobster 266

The Regional Specificity of Neural Induction 266

The head inducer: Wnt antagonists 266

Trunk patterning: Wnt signals and retinoic acid 269

Specifying the Left-Right Axis 270

EARLY ZEBRAFISH DEVELOPMENT 271

Cleavage 273

Gastrulation and Formation of the Germ Layers 275

Axis Formation 277

Dorsal-ventral axis formation 278

The fish Nieuwkoop center 279

Anterior-posterior axis formation 280

Left-right axis formation 280

Coda 282

CHAPTER 9

Early Development in Vertebrates

Birds and Mammals 285

EARLY DEVELOPMENT IN BIRDS 286

Cleavage 286

Gastrulation of the Avian Embryo 287

The hypoblast 287

The primitive streak 287

Molecular mechanisms of migration through the primitive streak 291

Regression of the primitive streak and epiboly of the ectoderm 292

Axis Specification and the Avian "Organizer" 293

The role of gravity and the PMZ 293

The chick"organizer" and the role of fibroblast growth factors 294

Anterior-posterior patterning 296 Left-right axis formation 297

EARLY MAMMALIAN DEVELOPMENT 298

Cleavage 298

The unique nature of mammalian cleavage 299

■ SIDELIGHTS & SPECULATIONS The Decisions That Really Shape Your Life 300

Compaction 301

Escape from the zona pellucida 303

Mammalian Gastrulation 303

Modifications for development inside another organism 303

SIDELIGHTS & SPECULATIONS Twins and Chimeras 304

Formation of the chorion 308

Mammalian Axis Formation 309

The anterior-posterior axis: Two signaling centers 309

Anterior-posterior patterning by FGF and retinoic acid gradients 310

Anterior-posterior patterning: The Hox code hypothesis 311

The dorsal-ventral and left-right axes 314

Coda 314

PART THREE THE STEM CELL CONCEPT

Introducing Organogenesis 319

The Stem Cell Concept 319
Stem Cell Vocabulary 321
Adult Stem Cells 322
Stem Cell Niches 322

Mesenchymal Stem Cells: Multipotent Adult Stem Cells 326 Pluripotent Embryonic Stem Cells 327 Stem Cell Therapy 328 A New Perspective on Organogenesis 331

CHAPTER 10

Emergence of the Ectoderm

Central Nervous System and Epidermis 333

NEURAL PLATE AND CENTRAL NERVOUS NEURAL PLATE AND CENTRAL NERVOUS SYSTEM 333

Formation of the Neural Tube 334

Primary neurulation 334 Secondary neurulation 339

Building the Brain 340

The anterior-posterior axis 341 The dorsal-ventral axis 343

Differentiation of Neurons in the Brain 345

Tissue Architecture of the Central Nervous System 347

Neural stem cell differentiation 347 Spinal cord and medulla organization 349 Cerebellar organization 350 Cerebral organization 351

Adult Neural Stem Cells 354

■ SIDELIGHTS & SPECULATIONS The Unique Development of the Human Brain 356

THE DYNAMICS OF OPTIC DEVELOPMENT: THE VERTEBRATE EYE 359

Formation of the Eye Field: The Beginnings of the Retina 360

The Lens-Retina Induction Cascade 362

Lens and cornea differentiation 364 Neural retina differentiation 364

THE EPIDERMIS AND ITS CUTANEOUS APPENDAGES 367

Origin of the Epidermis 367

The Cutaneous Appendages: Mammalian Hair 368

Hair follicles and hair generation in mammals 368 Adult stem cells and hair regeneration 369

Coda 372

CHAPTER 11

Neural Crest Cells and Axonal Specificity 375

THE NEURAL CREST 375

Specification of Neural Crest Cells 376
Regionalization of the Neural Crest 379

Trunk Neural Crest 380

Migration pathways of trunk neural crest cells 380 Mechanisms of trunk neural crest migration 380 The ventral pathway 382

The dorsolateral migration pathway 384

Cranial Neural Crest 386

Intramembranous ossification: Neural crest-derived head skeleton 388

Coordination of face and brain growth 390 Tooth formation 391

Cardiac Neural Crest 391

Cranial Placodes 392

NEURON SPECIFICATION AND AXON SPECIFICITY 394

■ SIDELIGHTS & SPECULATIONS The Growth Cone 394

The Generation of Neuronal Diversity 396

Pattern Generation in the Nervous System 398

Cell adhesion and contact guidance by attraction and repulsion 399

Membrane proteins: The ephrins and semaphorins 399

Guidance by diffusible molecules 400

Target selection 404

Synapse formation: Activity-dependent development 405

Differential survival after innervation: The role of neuroptrophins 405

Paths to Glory: The Travels of the Retinal Ganglion Axons 407

■ SIDELIGHTS & SPECULATIONS The Brainbow 409

CHAPTER 12

Paraxial and Intermediate Mesoderm 415

PARAXIAL MESODERM: THE SOMITES AND THEIR DERIVATIVES 416

Formation of the Somites 417

Where somites form: The Notch pathway 418 Separation of somites from the presomitic mesoderm 420

Periodicity of somite formation 420

■ SIDELIGHTS & SPECULATIONS Coordinating Waves and Clocks in Somite Formation 421

Epithelialization of the somites 423

Specification of the somites along the anteriorposterior axis 423

Differentiation of the somites 423

Determination of the sclerotome 426

Determination of the central dermamyotome 427

Determination of the myotome 428

Myoblasts and myofibers 429

Satellite cells: Unfused muscle progenitor cells 431

Osteogenesis: The Development of Bones 432

Endochondral ossification 432

Vertebrae formation 434

SIDELIGHTS & SPECULATIONS Mechanotransduction in the Musculoskeletal System 435

Tendon Formation: The Syndetome 436

Formation of the Dorsal Aorta 436

INTERMEDIATE MESODERM: THE UROGENITAL SYSTEM 436

The Progression of Kidney Types 438

Specification of the Intermediate Mesoderm: Pax2/8 and Lim1 439

Reciprocal Interactions of Developing Kidney Tissues 440

Mechanisms of reciprocal induction 441

Coda 447

CHAPTER 13

Lateral Plate Mesoderm and the Endoderm 449

FORMATION AND DEVELOPMENT OF THE CIRCULATORY SYSTEM 450

Heart Development 450

Formation of the heart fields 450 Specification of the cardiogenic mesoderm 451 Migration of the cardiac precursor cells 453 Heart cell differentiation 455
Fusion of the heart rudiments and initial heartbeats 456

■ SIDELIGHTS & SPECULATIONS A Minimalist Heart 457

Looping and formation of heart chambers 457

Blood Vessel Formation 460

Constraints on the construction of blood vessels 460

■ SIDELIGHTS & SPECULATIONS Redirecting Blood Flow in the Newborn Mammal 461

Vasculogenesis: The initial formation of blood vessels 463

Angiogenesis: Sprouting of blood vessels and remodeling of vascular beds 467

Arterial and venous differentiation 467

Organ-specific capillary formation 468

Anti-angiogenesis in normal and abnormal development 470

The lymphatic vessels 471

Hematopoiesis: The Stem Cell Concept 472

Sites of hematopoiesis 472

The bone marrow HSC niche 474

Hematopoietic inductive microenvironments 475 In conclusion 475

ENDODERM 476

The Pharynx 478

The Digestive Tube and Its Derivatives 478

Specification of the gut tissue 479 Liver, pancreas, and gallbladder 481

■ SIDELIGHTS & SPECULATIONS Specification of Liver and Pancreas 481

The Respiratory Tube 484 Coda 486

CHAPTER 14

Development of the Tetrapod Limb 489

Formation of the Limb Bud 490

Specification of the limb fields 490

Induction of the early limb buds: Wnt proteins and fibroblast growth factors 492

Specification of forelimb or hindlimb 492

Generating the Proximal-Distal Axis of the Limb 495

The apical ectodermal ridge 495

FGFs in the induction of the AER 496

Specifying the limb mesoderm: Determining the proximal-distal polarity of the limb skeleton 497

The dual-gradient model of limb patterning 497

■ SIDELIGHTS & SPECULATIONS A Reaction-Diffusion Mechanism for Building the Limb Skeletal Pattern 499

Specifying the Anterior-Posterior Axis 502

The zone of polarizing activity 502 Sonic hedgehog defines the ZPA 502 Specifying digit identity by Sonic hedgehog 504

SIDELIGHTS & SPECULATIONS Hox Gene Changes during Limb Development 506

Generation of the Dorsal-Ventral Axis 508

Coordinating the Three Axes 509

Cell Death and the Formation of Digits and Joints 510

Sculpting the autopod 510 Forming the joints 510

■ SIDELIGHTS & SPECULATIONS Evolution by Altering Limb Signaling Centers 512

Continued Limb Growth: Epiphyseal Plates 514

Fibroblast growth factor receptors: Dwarfism 514 Growth hormone and estrogen receptors 515 Parathyroid hormone-related peptide and Indian hedgehog 516

Coda 516

CHAPTER 15

Sex Determination 519

CHROMOSOMAL SEX DETERMINATION 519

The Mammalian Pattern 519

Primary Sex Determination in Mammals 522

The developing gonads 522

Genetic mechanisms of primary sex determination: Making decisions 524

The ovary pathway: Wnt4 and R-spondin1 525

The testis pathway 525

The right time and the right place 529

Secondary Sex Determination in Mammals: Hormonal Regulation of the Sexual Phenotype 530

The genetic analysis of secondary sex determination 531

Chromosomal Sex Determination in Drosophila 532

■ SIDELIGHTS & SPECULATIONS Brain Sex: Secondary Sex Determination through Multiple Pathways 533

The Sex-lethal gene 537

Doublesex: The switch gene for sex determination 539

Brain sex in *Drosophila* 540

Dosage Compensation 541

ENVIRONMENTAL SEX DETERMINATION 541

Temperature-Dependent Sex Determination in Reptiles 541

The aromatase hypothesis for environmental sex determination 542

Estrogens, aromatase, sex reversal, and conservation biology 542

Location-Dependent Sex Determination 544 Coda 545

CHAPTER 16

Postembryonic Development

Metamorphosis, Regeneration, and Aging 549

METAMORPHOSIS: THE HORMONAL REACTIVATION OF DEVELOPMENT 549

Amphibian Metamorphosis 550

Morphological changes associated with amphibian metamorphosis 550

Hormonal control of amphibian metamorphosis 553 Regionally specific developmental programs 555

■ SIDELIGHTS & SPECULATIONS Variations on the Theme of Amphibian Metamorphosis 556

Metamorphosis in Insects 558

Imaginal discs 559

Determination of the wing imaginal discs 562 Hormonal control of insect metamorphosis 564 The molecular biology of 20-hydroxyecdysone activity 565

REGENERATION 568

Stem-Cell Mediated Regeneration in Flatworms 569

Epimorphic Regeneration of Salamander Limbs 571

Formation of the apical ectodermal cap and regeneration blastema 571

Proliferation of the blastema cells: The requirement for nerves and the AEC 572

Regeneration in Hydra: Morphallaxis and Epimorphosis 574

The head activator 575

The head inhibition gradients 577

Compensatory Regeneration in the Mammalian Liver 578

AGING: THE BIOLOGY OF SENESCENCE 579

Genes and Aging 579

DNA repair enzymes 581

■ SIDELIGHTS & SPECULATIONS Exceptions to the Aging Rule 581

Aging and the insulin signaling cascade 582 The mTOR pathway 583 Chromatin modification 583 Integrating the conserved aging pathways 584

■ SIDELIGHTS & SPECULATIONS Young Blood: Serum Factors and Progenitor Cells 585

Environmental and Epigenetic Causes of Aging 586

Promoting Longevity 587

CHAPTER 17

The Saga of the Germ Line 591

Conserved Molecular Components 591 Germ Cell Specification 592

Germ cell determination in nematodes 592 Germ cell determination in insects 594 Germ cell determination in frogs and fish 596 Germ cell determination in mammals 596 The inert genome hypothesis 597

■ SIDELIGHTS & SPECULATIONS Pluripotency, Germ Cells, and Embryonic Stem Cells 598

Germ Cell Migration 601

Germ cell migration in *Drosophila* 601 Germ cell migration in vertebrates 603

The Primacy of Meiosis 606

■ SIDELIGHTS & SPECULATIONS Big Decisions: Mitosis or Meiosis? Egg or Sperm? 608

Gamete Maturation 610

Maturation of the oocytes in frogs 610 Meroistic oogenesis in insects 613

Gametogenesis in Mammals 614

Spermatogenesis 616 Oogenesis in mammals 619

Coda 623

PART FOUR

SYSTEMS BIOLOGY

Expanding Developmental Biology to Medicine, Ecology, and Evolution 627

Pragmatic Systems Biology: From Gene to System 627

Systems Theory Biology: From System to Gene 630

Context-Dependent Properties 631

Level-Specific Properties and Emergence 631

Heterogeneous Causation 632

Integration 632

Modules and Robustness 632

Homeorhesis 633

CHAPTER 18

Birth Defects, Endocrine Disruptors, and Cancer 635

The Role of Chance 635

Genetic Errors of Human Development 636

The nature of human syndromes 637 Genetic and phenotypic heterogeneity 637

Teratogenesis: Environmental Assaults on Human Development 638

Alcohol as a teratogen 640 Retinoic acid as a teratogen 642 Other teratogenic agents 643

Endocrine Disruptors: The Embryonic Origins of Adult Disease 644

■ SIDELIGHTS & SPECULATIONS Developmental Origins of Adult-Onset Disease 645 DES as an endocrine disruptor 647

SIDELIGHTS & SPECULATIONS Testicular Dysgenesis Syndrome 649

Bisphenol A (BPA) 652

Endocrine disruptors as obesogens 654

Transgenerational Inheritance of Developmental Disorders 654

Cancer as a Disease of Development 655

Context-dependent tumors 656

Cancer stem cells and the epithelial-mesechymal transition 658

Cancer and epigenetic gene regulation 659 Developmental therapies for cancer 659

Coda 660

CHAPTER 19

Ecological Developmental Biology

Biotic, Abiotic, and Symbiotic Regulation of Development 663

The Environment as a Normal Agent in Producing Phenotypes 663

Diet-induced polyphenisms 665 Predator-induced polyphenisms 667 Temperature as an environmental agent 669

Environmental Induction of Behavioral Phenotypes 671

Adult anxiety and environmentally regulated DNA methylation 671

Learning: The Developmentally Plastic Nervous System 672

Experiential changes in mammalian visual pathways 673

Life Cycles and Polyphenisms 674

Diapause 674

Larval settlement 675

■ SIDELIGHTS & SPECULATIONS Life Cycle Choices: Dictyostelium 676

The hard life of spadefoot toads 679

Developmental Symbioses 680

Mechanisms of developmental symbiosis: Getting the partners together 680

The Euprymna-Vibrio symbiosis 682

Obligate developmental mutualism 682

Developmental symbiosis in the mammalian intestine 684

Coda 686

CHAPTER 20

Developmental Mechanisms of Evolutionary Change 689

Descent with Modification: Why Animals Are Alike and Different 689

■ SIDELIGHTS & SPECULATIONS Development, Multicellularity, and the Origin of the Metazoa 690

Preconditions for Evolution: The Developmental Structure of the Genome 690

Modularity: Divergence through dissociation 691 Molecular parsimony: Gene duplication and divergence 694

Deep Homology 698

Mechanisms of Evolutionary Change 699

Heterotopy 699 Heterochrony 701 Heterometry 702 Heterotypy 705

■ SIDELIGHTS & SPECULATIONS Transposable DNA Elements and the Origins of Pregnancy 706

Developmental Constraints on Evolution 708

Physical constraints 708 Morphogenetic constraints 708 Phyletic constraints 708

■ SIDELIGHTS & SPECULATIONS Reaction-Diffusion Kinetics and the Evolution of Mammalian Teeth 709

Selectable Epigenetic Variation 711

Genetic assimilation 713

Fixation of environmentally induced phenotypes 715

■ SIDELIGHTS & SPECULATIONS Hsp90 and Genetic Assimilation 716

Coda 716

GLOSSARY G-1

CHAPTER-OPENING SOURCE CREDITS C-1

AUTHOR INDEX AI-1

SUBJECT INDEX SI-1